With Compliments.

TUBERCULAR IRITIS.

By W. B. INGLIS POLLOCK, M.B., Ch.B.,

Clinical Assistant, Glasgow Eye Infirmary ; Member of the Ophthalmological Society of the United Kingdom.

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TUBERCULAR IRITIS is only given a small place in the current text-books of diseases of the eye. Many deny its existence, except in a small percentage of cases. This is due to the lack of absolute proof in so many instances, as both clinically and pathologically the opportunity for microscopic or inoculation tests is rare, and the difficulty of a positive result is sometimes great. V. Michel[2] (1881) was the first to insist on the relative frequency, yet Axenfeld[3] (1901) and Ginsberg[4] (1903), in his text-book of pathological anatomy of the eye, hold that many cases of iritis must not be attributed to tuberculosis without actual proof.

I am indebted to Professor Greef, director of the eye department in the Charité, Berlin, for the eyeball from the following case, and for permission to use it and the clinical notes of the case:—

Alice L., æt. 16, without any occupation, was admitted on 1st March, 1901, into the eye department of the Charité, Berlin.

She was the illegitimate child of a ballet-girl who had died ten years previously of consumption. She herself, apart from repeated colds, had not suffered from any severe illness. Since childhood her sight and hearing had been bad. Two years previously she had been in the Charité for a short time on account of severe interstitial keratitis in the right eye, followed by a milder attack in the left. A course of mercurial

[1] Read at a meeting of the Glasgow Pathological and Clinical Society held on 9th November, 1903.

[2] V. Michel, v. Graefe's *Arch. f. Ophth.*, 1881, Bd. xxvii.

[3] Axenfeld, *Allgemeine Pathologie und pathologische Anatomie des Auges*, from Lubarsch-Ostertag's *Ergebnisse der allgemeinen Pathologie*, VI Jahrgang.

[4] Ginsberg, *Grundriss der pathologischen Histologie des Auges*, 1903.

inunction, iodides, and baths had failed to produce any improvement. Twice later this treatment was repeated, with the same result. This time she was admitted on account of great diminution in the vision of the left eye.

Condition on admission.—Patient is a weakly girl, of pale colour, and badly nourished. Deafness, due to labyrinthine disease, requires words to be spoken directly into the ears. The teeth are of a dirty colour, but show no notching or stunting in the incisors. The chest is flat and depressed in the infra-clavicular region. Over the right apex is diminished movement, altered percussion note, bronchial breathing, but no râles; otherwise healthy.

In left eye there is severe pericorneal injection, ciliary tenderness on pressure, and the cornea is obscured by a slight breath-like opacity, into which blood-vessels run. The surface is flat. The iris and pupil are fairly easily seen. The latter is small and irregular, with posterior synechiæ, and does not respond to light. The iris is discoloured and its surface markings are almost entirely effaced. Near the pupillary margin, along the smaller arterial circle of the iris, are seven or eight small millet seed-like nodes, of a grey colour, projecting above the surface. No vessels enter them. They are all below the level of the upper edge of the pupil. The fundus cannot be detected in detail. Tension is slightly minus: V.A. = $\frac{1}{15}$.

In right eye there is also considerable pericorneal injection, but cornea is more opaque than the left, and development of vessels greater. Four or five nodes are seen in about the same situation of the iris as in the left eye, but no further details are visible on account of the opacity. Tension normal; V.A. = $\frac{1}{20}$.

Course of the disease.—Treatment: rest, atropin, and warm fomentations to allay the irritation. As the pupils remained fixed, and the tension rose in both eyes, a superior iridectomy was performed in right on 11th and in left on 19th March. Wounds healed regularly, and only in left appeared slight signs of reaction. By 1st April the condition was unchanged—right had V.A. = $\frac{1}{20}$. Left, still great injection. The surface markings of the iris were obliterated. Nodes not so distinct. Tension minus. V.A., left = movements of hand at 2 feet. On 20th April a course of mercury and iodides was commenced, but given up on 20th May, as no improvement had occurred. V.A., right = $\frac{1}{10}$; V.A., left = fingers at 2 feet. By 1st July a greyish-white node formed in the upper margin of the right cornea. The nodes on the iris had become less distinct.

Tension was decreased, and slightest pressure on the globes caused pain. The right remained unchanged, but left became softer and more painful and inflamed, so on 27th July the left eye was enucleated.

She was dismissed on 11th September with V.A., right = fingers at 3½ feet, and tension minus also.

The left eyeball was placed in Müller's fluid and preserved in 70 per cent alcohol, then embedded in celloidin for cutting into sections.

Naked-eye examination.—The anterior chamber is shallow; the vitreous shrunken to two-thirds; the retina in position; and a number of tubercles the size of pinheads visible in the choroid. A slightly larger one, lying at the inferior part, I returned to Professor Greef for the museum.

Microscopic examination.—There are numerous broad peripheral adhesions of the iris to the cornea, but internally and superiorly the angle of the anterior chamber is free. At almost all parts the iris is attached to the anterior surface of the lens at the pupillary margin (posterior synechiæ). A fine connective tissue membrane lies across the pupil, representing an exudation of some considerable age, which has been replaced by fibrous tissue. That its origin is not very old is shown by the presence of oval cells which are passing into spindle cells, and by the absence of shrinking. At the centre of the lens it is thicker, but for the most part it is little more than a single layer of cells. There is considerable bulging of the iris forwards near its peripheral attachment, a condition termed clinically "iris bombé." All these show that increased tension has caused the destruction of the eyeball, and led to the atrophy of the ciliary body to be described.

The nodules projecting on the surface of the iris are composed of epithelioid and round cells, the latter in predominance. They have no capsule nor vessels in the interior. Giant cells and tubercle bacilli were not found. Other nodes lie deep in the stroma of the iris, and a number are present near the periphery of the anterior chamber in the ligamentum pectinatum or the iris. Most of them lie about one to two millimetres from the pupillary margin. No caseation was noted. The remaining changes in the iris are mainly those of atrophy. The delicate reticulated stroma of branching cells has been almost entirely lost, especially in the ciliary zone, and is replaced by a tissue rich in round- and spindle-shaped elements. The posterior pigment layer is in position. Small hæmorrhages are seen at one or two places (Fig. 1, p. 4).

In the ciliary body are also seen the same circumscribed

aggregations of cells, some even in ciliary processes, but the most marked change is the atrophy of the various structures, the ciliary muscle and the ciliary processes, accompanied by a connective tissue increase.

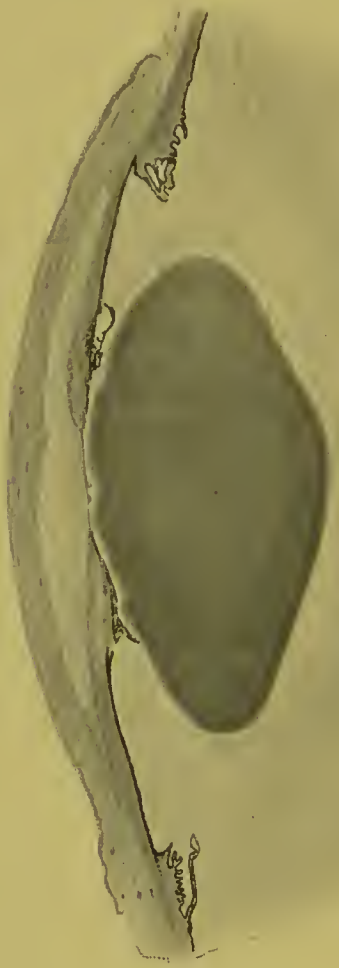


FIG. 1.

Anterior segment of eyeball through the pupil, showing at the lower angle the peripheral adhesion of iris to cornea, the pupillary membrane, the posterior synechiæ, and atrophy of the ciliary body. The lens has been dislocated backwards artificially, and this brings out well the pupillary membrane. No nodes. (× 12 diam.)

The cornea is the seat of an infiltration of round cells lying between the lamellæ, with the presence of numerous blood-vessels. The lamellæ look as if replaced by connective tissue at many spots. These changes are most marked in the posterior layers. Bowman's membrane is interrupted at many

places with some irregularity of the epithelium and of the subjacent corneal lamellæ. Descemet's membrane is normal, only showing an artificial fold near the centre. The epithelium lining it is in position, and here and there a few cells are seen adhering to its posterior surface. No tubercles or giant

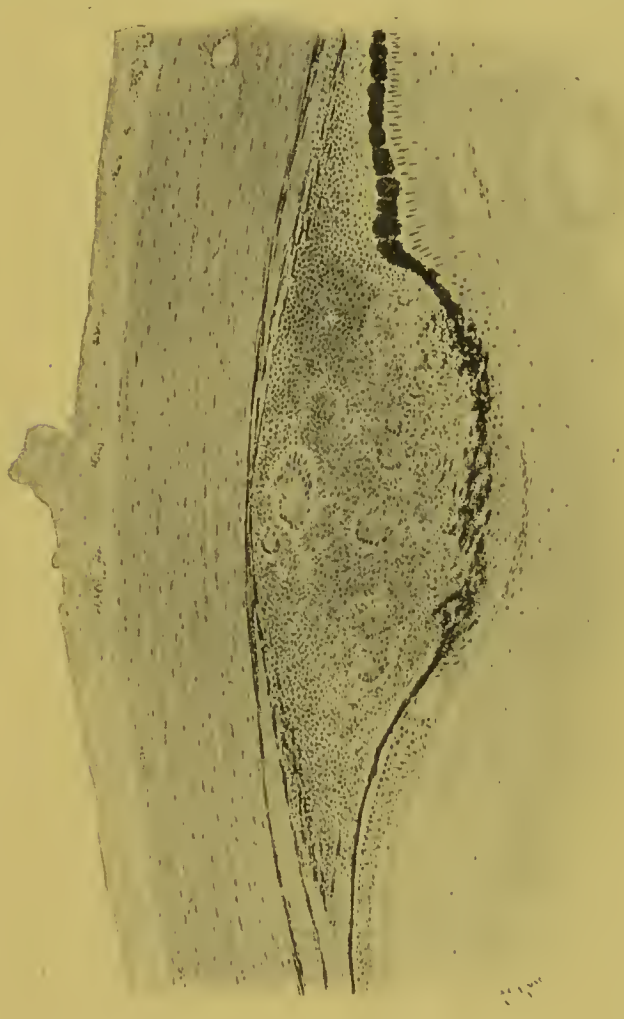


Fig. 2.

A tubercle in the choroid with several giant cells. (× 80 diam.)

cells were found, although several of the former are seen in the spaces of Fontana, as already mentioned. The lens shows several artificial breaks, but is otherwise normal. An albuminous exudation fills the anterior chamber, and a layer of fibrin and cells entangled in it is lying in front of the

pupillary membrane. There is also a great increase of albumen in the vitreous, with a few round cells between the ciliary processes (Fig. 2, p. 5). The choroid shows numerous tubercles, with centrally-placed giant cells surrounded by epithelioid and, in the periphery, round cells. They project towards the retina, bulging it inwards. The pigment layer is broken up and increased or absorbed. The retina over the tubercles is attached, and its external layers degenerated. At other places in the choroid there are intense collections of small round lymphocytes. At the posterior pole the vessels are greatly dilated, and near the optic nerve entrance is another tubercle. No caseation nor tubercle bacilli were found. The retina, apart from changes noted, is normal. There is slight œdema of the disc, but the optic nerve is normal. Around the vessels penetrating the sclerotic are numerous lymphocytes.

Iritis, accompanied by nodules, may be syphilitic, tubercular, sympathetic, leukæmic, or due to presence of caterpillar hairs, or finally result from some possible general inflammatory action, the nature of which we do not know. In the present case sympathetic disease can be neglected, nor does this case give any support to the recent hypothesis of Peters[1] that many cases of sympathetic disease are tubercular. The other etiological factors, except syphilis and tuberculosis, may also be set aside.

In favour of a diagnosis of congenital syphilis are the following:—She was the illegitimate child of a ballet-girl; the opportunity for infection therefore cannot be denied. She had great deafness, and during the last two years suffered from interstitial keratitis, but the teeth showed none of the characteristics described by Hutchinson.[2] The deafness was due to labyrinthine disease, and most probably, but not demonstrably, syphilitic. Keratitis interstitialis may result from other causes than syphilis, notably tuberculosis, as in a case of v. Hippel's,[3] which had been diagnosed clinically as specific, but pathologically showed numerous typical tubercles in the iris and other parts, but no bacilli. The cases of Schultze[4] and Zimmermann[5] also dispose of Hutchinson's[6]

[1] Peters, *Zeitschrift f. Augenheilk.*, 1901.
[2] Hutchinson, *Syphilis*, 1887.
[3] V. Hippel, v. Graefe's *Arch. f. Ophth.*, 1893, Bd. 39.
[4] Schultze, *Arch. f. Augenheilk.*, 1896, Bd. 33.
[5] Zimmermann, v. Graefe's *Arch. f. Ophth.*, 1895, Bd. 41.
[6] Hutchinson, *loc. cit.*

statement that interstitial keratitis, in its typical form, is always a consequence of syphilis, and sufficient for a diagnosis.

The reasons for the diagnosis of tuberculosis were the following:—In the present case, continued treatment by mercury and iodides failed to give any improvement in either corneal or iritic condition.

Syphilitic nodules are usually found at the pupillary margin, and very rarely in the body of the iris; they are often reddish in colour, and limited to one or two in number. The tubercles in the present instance were greyish, numerous, and situated along the line of the lesser arterial circle. Histologically they are composed of the same elements as may occur in syphilis or tuberculosis. Those found in the deeper parts of the eye showed the structure of tubercles in every respect. They have the characteristic giant cells with marginal nuclei, the branching processes, the epithelioid cells, and the marginal accumulation of small round cells. Can syphilis produce such a picture as seen in Fig. 2 (p. 5)? A few pathologists think so. None of the reported cases of syphilis in the eye show any lesion like it, except a case of Peppmüller's,[1] which he believed to be syphilitic, and his argument rests on rapid healing after potassium iodide, although tubercle bacilli were found and the inoculation test was successful.

The absence of caseation is unimportant—either this case may have been passing into a fibroid condition, or simple disappearance of tubercles was occurring. Regarding the failure to find tubercle bacilli, it need hardly be mentioned how difficult it is to discover them in certain admittedly tubercular lesions, and this is true even where one has injected the bacilli; but where tissue has lain, as this eye did, in Müller's fluid for a lengthened period, it is almost impossible. I stained twenty-five sections without finding them, and then the attendant did another six also unsuccessfully. Hill Griffith,[2] after a review of thirty-two cases of tubercular iritis, says that "the value of this test is only great where the results are positive, as failure is so very common even in the hands of competent men." Professor Dresfeld examined for them in his case without success. Leber[3] has also shown how cases, even in spite of the absence of giant cells, of the

[1] Peppmüller, v. Graefe's *Arch. f. Ophth.*, 1899, Bd. 49, part 2; reference, Axenfeld, *Ergebnisse.*

[2] Hill Griffith, *Trans. Ophth. Soc. United Kingdom*, 1890.

[3] Leber, *Bericht der Ophth. Gesellschaft. zu Heidelberg*, 1891.

discovery of bacilli, and the failure of the inoculation test, may yet be tubercular. The tissue of the present case had lain too long in alcohol to be available for inoculation.

Looking at the nodes in the iris, in the ciliary body, pectinate ligament, and in the choroid, in fact the whole uveal tract, one is forced to the diagnosis of the same process in each constituent, since each is so liable to be involved in any inflammation in another; they have the same blood and nerve supply. The nodes in the anterior segment are less developed, or they have passed beyond the typical stage. As regards the tubercles in the choroid, almost all pathologists will acknowledge they are tubercular. We have then a tubercular invasion of the whole uveal tract: and, in view of the clinical history, I am inclined to think that the choroidal affection is possibly later. It was five months after the admission of the patient before the enucleation was performed, and in that time the nodules in the iris had slowly subsided and lost their distinct prominence. Those in the choroid were not advanced enough for caseation.

In support of this diagnosis there are a few additional points. The cornea at numerous places indicates shallow losses of substance which have healed, and that several years ago, as the surface was quite flat. They must have been ulcers, and were in all probability phlyctenular. This accounts for the dimness of sight since childhood, and would be consistent with a strumous diathesis. The patient was 16, and Hutchinson [1] describes cases of iritis in congenital syphilis as occurring in infancy, and being very susceptible to treatment. The patient's chest had the tubercular appearance, if one may say so, and the right apex was affected. Her mother had died ten years previously of consumption.

Greef [2] differentiates three forms of tuberculosis of the iris; the two first are due to Haab,[3] and the third to v. Michel [4]:—

1. Miliary tuberculosis, in which tubercles are observed on the surface of the iris. Leber [5] called it "attenuated tuberculosis," on account of the recovery, which often occurs by the process subsiding spontaneously, and the absence of any

[1] Hutchinson, *loc. cit.*
[2] Greef, "Die pathologische Anatomie des Auges," Orth's *Lehrbuch der spec. path. Anat.*, 1902.
[3] Haab, v. Graefe's *Arch. f. Ophth.*, 1880, Bd. 25.
[4] Michel, *loc. cit.*
[5] Leber, *loc. cit.*

tendeney to form large nodes. It has nothing to do with attenuation of the baeilli, as Samelsohn [1] showed by experiments and elinieal cases. The disease may lead to destruetion of the eye, either by the shrinking of a plastie irido-eyelitis or oeeasionally from a glaueomatous eondition. Here rise of tension oecurred early in the disease, but after an irideetomy, whieh healed normally, there set in a progressive painful softening, associated with the atrophy of the ciliary body, which led to the enucleation.

2. The solitary or eonglomerate tuberele, whieh slowly inereases in size, and ultimately almost invariably leads to destruetion of the eye, either by shrinking or more eommonly by perforation. Enucleation requires to be performed in every ease.

3. Simple tubereular iritis. Clinieally it shows no distinetions from syphilitie iritis, but mieroseopieally typieal tubereles are found lying in the stroma of the iris. Axenfeld [2] deelines to aeeept this one, exeept in so far as it is a stage of the first, but v. Michel and his pupils elaim that there are such cases, and that they run a eourse the same as the ordinary iritis without nodules, and the diagnosis rests mainly on the general eondition. It is over this form that there is so much eontention, and it is not yet settled.

The different forms may pass into one another, and sometimes are not to be sharply separated. Two of Samelsohn's [3] cases, whieh were dismissed healed from miliary tuberculosis, returned later with a graver form, and died by meningitis shortly afterwards.

Most now agree that tubercular iritis is seeondary, in so far that the virus, apart from trauma, must come through the body. Still, the souree of infection may have quietened down, and only the eye remain aetive. Baeilli are swept through the filtration angle, where tubercles so often oeeur, into the eirculation. Tuberculosis of the eye, however, frequently remains loeal, as in bone or joint disease. The older view of enueleation in every ease, undoubtedly, saved lives, but it is being given up. In the miliary form eonservative treatment has taken its place—atropin, fomentations, and sedatives if necessary. Tubereulin has been tried by some with varying results, but is viewed sceptically by most surgeons. Irideetomy has also been done in Griffith's series [4]

[1] Samelsohn, *Bericht der Ophth. Gesellschaft. zu Heidelberg*, 1893.
[2] Axenfeld, *loc. cit.*
[3] Samelsohn, *loc. cit.*
[4] Hill Griffith, *loc. cit.*

eight times, but in each case the eyeball had subsequently to be enucleated. If one remembers the tubercles in the stroma, and hidden at the angle of the anterior chamber, no astonishment need be expressed over this result. Enucleation is to be reserved, then, for cases in which other treatment has failed and the eye is useless for vision, where there is danger of sympathetic disease, or where the tubercular lesion is an advancing destructive one. These indications I owe to Hill Griffith.[1]

To enable us to come to a surer diagnosis, and lead to further accuracy, there should be more routine examination of the excised portion of iris in all old-standing cases of iritis. This position is held by most continental workers, and although difficult, yet it is sure to widen knowledge if followed with care.

Postscript.—Since writing the above, I have read a very suggestive paper by Darier,[2] of Paris, communicated to the Ophthalmological Section of the British Medical Association, 1903, on the treatment of interstitial keratitis by tuberculin T.R. He mentions a number of remedies, and some of these might be tried in tubercular iritis.

[1] Hill Griffith, *loc. cit.*
[2] Darier, *Ophth. Review*, December, 1903.

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